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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/444,144	11/20/99	HOWELL M	CYT0001

HM12/0810

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EXAMINER	
HELMS,L	
ART UNIT	PAPER NUMBER
1642	23

DATE MAILED: 08/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/444,144	Applicant(s) HOWELL ET AL.	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34,37,38,40-42 and 50-56* is/are pending in the application.

4a) Of the above claim(s) *4,6-9 and 28-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,10-27,34,37,38,40-42 and 50-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The indicated allowability of claims 1-34, 37-38, 40-42, 50-56 is withdrawn in view of the newly submitted IDS (paper # 22). Rejections based on the newly cited reference(s) follow.

2. Claims 1-3, 5, 10-27, 34, 37-38, 40-42, and 50-56 are under examination and will be examined to the extent they read on the species elected in paper # 6 as:inert medium of a macroporous bead, inhibitor of soluble receptors for tumor necrosis factor alpha, and binding partner is an antibody.

3. Claims 4, 6-9, 28-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains some NEW GROUNDS of rejection.

Claim Rejections - 35 USC § 103

6. Claims 1-3, 5, 10-27, 34, 37-38, 40-42, 50-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (U.S. Patent 6,231,536, filed 5/21/99, IDS #12) and further in view of Selinsky et al (Immunology 94:88-93, 5/1998, IDS #4) and Maraskovsky et al (U.S. Patent 6,017,527, filed 12/12/96).

The claims are summarized as a method of stimulating an immune response in a mammal having a pathological condition comprising obtaining blood from the mammal

or human and separating the whole blood into cellular components and a plasma component, contacting the plasma with a recombinant monoclonal or polyclonal antibody or a plurality of such which is covalently attached to a macroporous bead specific for soluble receptors for tumor necrosis factor alpha and the antibody-immune system inhibitor is removed by mechanical or biological or chemical means and combining the cellular component and administering the whole blood to the mammal.

Lentz teach a method and system for removing immunosupressive components from the blood of mammals for treating diseases and conditions in deficiencies in the immune response system and the treated blood is returned to the patient to initiate an immune response (see abstract). Lentz teach the methods can treat cancer and tumors (column 1, lines 63-64) and the method removes soluble receptors for TNF (see column 2, lines 10-22) and the blood cells and returned to the patient (see column 2). Lentz teach removal of soluble receptor/inhibitors to sTNFR-1 and sTNFR-2 which may restore the immune systems attack on the tumor cells (see colunm 1, lines 46-51 and column 2, lines 11-15). Lentz teach the patient can be a human and the treatment can be performed multiple times with the blood. Lentz teach removal of immunosupressive components with Ultrapheresis and an antibody immobilized using standard techniques for binding reactions to remove proteins from the blood (see column 7, lines 5-18). Lentz does not specifically teach a recombinant monoclonal antibody specific for soluble receptors for tumor necrosis factor alpha covalently joined to a macroporous bead. These deficiencies are made up for in the teachings of Selinsky et al and Maraskovsky et al.

Selinsky et al teach antibodies specific for sTNFRI and Ultraphoresis which is a system that selectively removes plasma components within a defined molecular range which have been implemented as inhibitors of the inflammatory response (see page 88,

introduction). Selinsky et al also teach soluble tumor necrosis factor receptor type I is removed by Ultrapheresis (see page 880) and sTNFRI effectively inhibits immune responses in vivo and demonstrates that modulation is a legitimate therapeutic avenue and an anti-human sTNFRI antibody (see page 89 and 92). Selinsky et al also teach "We, therefore, propose the development of methods and/or reagents capable of specifically removing sTNFRI, or antagonizing its effects in situ, as unconventional, yet promising, strategies for cancer immunotherapy." (See page 92).

Maraskovsky et al teach a method of stimulating an immune response in a patient providing a method in which antibodies specific to antigens are immobilized onto a surface such as beads and the blood cells are collected by aphoresis (see column 3, lines 55-56) and the monoclonal antibodies which can be recombinant (column 8, lines 20-21) remove the specific cells and the antibody-antigen complex is removed by a column chromatography method or biological method (see column 4, lines 38-49) and the cells are administered to the patient.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the method of Lentz to stimulate an immune response with antibodies to sTNFRI for removal of sTNFRI which inhibits the immune response as taught by Selinsky et al and Lentz and immobilize the antibody to a macroporous bead as taught by Maraskovsky et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success in having used the method of Lentz to stimulate an immune response with antibodies to sTNFRI as taught by Selinsky et al and immobilize the antibody to a macroporous bead as taught by Maraskovsky et al because Lentz teach a method of stimulating an immune response with removal of immune system inhibitors, sTNFR-1 and 2, with an immobilized antibody to these components and both

Lentz and Selinsky et al teach that sTNFRI is removed from blood and that sTNFRI inhibits the immune response. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success in combining the teachings of Lentz, Selinsky et al and Maraskovsky et al because Selinsky et al teach "We, therefore, propose the development of methods and/or reagents capable of specifically removing sTNFRI, or antagonizing its effects in situ, as unconventional, yet promising, strategies for cancer immunotherapy." (See page 92). Moreover, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success in combining the teachings of Lentz, Selinsky et al and Maraskovsky et al because Maraskovsky et al teach antibodies immobilized on a bead for removal of antigens from a blood sample and administering the altered blood sample to the individual to enhance an immune response. In addition, it would have been obvious to use either a polyclonal antibody or a monoclonal antibody as well as a panel of antibodies that are specific for either one immune system inhibitor or several immune system inhibitors for Lentz teach that there are immunosupressive components in the blood which were separated. In addition, one skilled in the art would know to remove the antibody/antigen complex prior to administering the biological fluid to the patient. Thus, it would have been obvious to use the method of Maraskovsky et al to immobilize an antibody of Selinsky which specifically binds to sTNFRI, wherein the sTNFRI inhibits the immune response, and is removed in the method of Lentz using an immobilized antibody.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

7. No Claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

SHEELA HUFF
PRIMARY EXAMINER

Respectfully,

Larry R. Helms Ph.D.

703-306-5879